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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/161,680	09/28/1998	UWE BORNSCHEUER	48429	7944

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EXAMINER

STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
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1656

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

09/161,680

Applicant(s)

BORNSCHEUER ET AL.

Examiner

David J. Steadman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 May 2006 and 25 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12,13,15 and 19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12,13,15 and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date. 20070205.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status of the Application

- [1]** Claims 12-13, 15, and 19 are pending in the application.
- [2]** Applicant's amendment to the claims, filed on 5/8/06, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.
- [3]** Applicant's amendments to the specification, filed on 5/8/06 and 9/25/06, are acknowledged. The specification amendment filed on 5/8/06 fails to satisfy the requirements of 37 CFR 1.121 for the reason(s) noted in the Office communication mailed on 7/25/06. The specification amendment filed on 9/25/06 appears to correct the noted defect(s).
- [4]** Applicant's arguments filed on 5/8/06 in response to the Office action mailed on 2/8/06 have been fully considered and are deemed to be persuasive to overcome some of the objections and/or rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [5]** The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Specification

- [6]** The objection to the specification as introducing new matter in the amendments to the specification filed on 4/15/2003, 9/16/2003, and 11/6/2003 is withdrawn in view of the substitute specification filed on 9/25/06, which appears to remove the new matter as cited in the Decision on Appeal mailed on 9/29/2005 at pp. 12-14.

Claim Rejections - 35 USC § 112, Second Paragraph

[7] The rejection of claims 12-13, 15, and 19 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "the alteration in substrate specificity leads to a stereoselective enzymatic activity" is withdrawn in view of applicant's arguments and supporting references.

RESPONSE TO ARGUMENT: Applicant argues there are numerous references in the prior art that teach non-specific enzymatic activity, citing Winkler and Markovitz as an example thereof, and thus, an enzymatic reaction is not necessarily stereoselective. Applicant argues the examiner has taken the teachings of Solomon out of context, asserting that Solomon's teachings are directed to enzymes in their natural environment. Applicant appears to dispute the teachings of Solomon, asserting that not all enzymes are stereoselective in their natural environment, citing desaturases as an example. Applicant further argues that the Solomon teachings are non-analogous as the invention is directed to stereoselectivity of an enzyme in *in vitro* reaction solutions.

Although Solomon teaches, "[t]he enzyme-catalyzed reaction is said to be stereoselective" (p. 167, bottom), in view of applicant's remarks, there would appear to be at least one isolated example of an enzyme wherein the reaction is not stereoselective and the examiner can proffer no evidence to suggest otherwise. As such, the term "the alteration in substrate specificity leads to a stereoselective enzymatic activity" has been interpreted as meaning the alteration results in an altered substrate specificity of the recited lipases, esterases, nitrilases, or phytases, wherein

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the altered substrate specificity results in a stereoselective enzymatic activity. It is noted that the term "leads to a stereoselective enzymatic activity" has been interpreted as meaning that the alteration results in a stereoselective enzymatic activity where none previously existed, or that the alteration results in a more stereoselective enzymatic activity relative to the respective enzyme activity prior to alteration.

Claim Rejections - 35 USC § 103

[8] The rejection of claim(s) 12-13 and 15 under 35 U.S.C. 103(a) as being unpatentable over Greener et al. (*Methods Mol Biol* 57:375-385, cited on the 11/30/1999 Form PTO-1449) in view of Short et al. (US Patent 5,830,696) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues that the Short et al. reference discloses "nothing more than a wish list of enzymes 'which may be mutagenized,'" asserting that "the data in the article appears to merely suggest an invitation to explore and as such, is not obvious," citing *Ex parte Obukowicz*, 27 USPQ2d 1063.

Applicant's argument is not found persuasive. In *Ex parte Obukowicz*, the Court held that "[w]e are unable to find a suggestion [in the prior art] to do what appellants have done" (emphasis original). Although applicant appears to take the position that the Short et al. reference, by providing a list of enzymatic activities that can be altered according to the disclosed method, is only an invitation to explore and not a suggestion to actually mutate these enzymes, it is noted that applicant's cited reference of Drauz

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and Waldmann (1995) acknowledges pig liver esterase as a prior art-recognized example of an enzyme catalyst in organic syntheses and further acknowledges "the skilled artisan would have known at the time of filing that the stereoselectivity in enzymatic catalysts in *in vitro* reaction solutions "is a major concern" (sentence bridging pp. 5-6). Contrary to the facts in *Ex parte Obukowicz*, the Short et al. reference at columns 6-7 provides an *express suggestion* to modify lipases, esterases, and nitrilases and an *express suggestion* of an activity to be altered, *i.e.*, substrate stereoselectivity. For example, under the listing "Lipase/Esterase," the Short et al. reference lists the activity to be modified as "Enantioselective hydrolysis of esters (lipids)/thioesters" (column 6, lines 32-33). As such, the examiner maintains that the claimed invention, in view of the combination of cited references, would have been obvious to one of ordinary skill in the art at the time of the invention.

[9] The rejection of claim 19 under 35 U.S.C. 103(a) as being unpatentable over Greener et al. in view of Short et al. as applied to claims 12-13 and 15 above and further in view of van der Kaay (*Biochem J* 312:907-910) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues the examiner has misread the 11/3/05 response, asserting this remark was directed to the claimed invention and "[a]t no point did the Applicants assert that any method, other than that disclosed, would be 'routine.'" Applicant further argues that the van der Kaay reference would not provide a

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skilled artisan with an expectation of success for practicing the claimed invention in view of the reference's teaching that "most InsP6-degrading enzymes are either not very specific or degrade InsP6 only at one position" and that the disclosed data are "based on a fortuitous discovery by a separate researcher."

Applicant's argument is not found persuasive. Regarding applicant's remark at p. 5, top of the 11/3/05 response, it is noted that the rejection using the combination of references is directed to the *claimed invention*. Thus, since the rejection is directed to the *claimed invention*, applicant's remark is considered relevant to the expectation of success for practicing the claimed invention as applicant clearly acknowledges "the experimentation required for claims 12-19 would be a routine matter for the skilled artisan."

Regarding the teachings of van der Kaay et al., the reference acknowledges that a problem with investigating routes of InsP6 synthesis is that "most InsP6-degrading enzymes are either not very specific or degrade InsP6 only at one position." In overcoming this problem, the reference suggests that "[i]nvestigations of the routes of InsP6 synthesis would be helped by the availability of enzymes that dephosphorylate InsP6 in a position-specific order," which "would allow us to follow the kinetics of incorporation and release of radioactive phosphate at each position of the molecule..." (p. 907, left column, middle). Thus, applicant's cited teaching of van der Kaay et al. along with other teachings in the reference, provide an *express suggestion* to obtain "enzymes that dephosphorylate InsP6 in a position-specific order," albeit van der Kaay et al. does not suggest obtaining such enzymes by the method of Short et al. However,

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at the time of the invention one of ordinary skill in the art would have recognized that such enzymes can be achieved by the method of Short et al., particularly as Short et al. provides an *express suggestion* to modify phosphatases (column 7, line 3) and, as acknowledged by applicant, the experimentation required to modify such a phosphatase is "a routine matter for a skilled artisan" as noted above.

As such, the examiner maintains that the claimed invention, in view of the combination of cited references, would have been obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

[10] Status of the claims:

Claims 12-13, 15, and 19 are pending.

Claims 12-13, 15, and 19 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.
Primary Examiner
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